510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k041799

B. Purpose for Submission:
Seeking 510(k) clearance of new hsCRP assay with the cardiac indications for use based on literature studies and comparable performance to the predicate device.

C. Analyte:
C-reactive protein

D. Type of Test:
Immunoturbidimetric assay

E. Applicant:
ORTHO-CLINICAL DIAGNOSTICS, INC.

F. Proprietary and Established Names:
VITROS CHEMISTRY PRODUCTS HSCRP REAGENT, VITROS CHEMISTRY PRODUCTS CALIBRATOR KIT 17, VITROS CHEMISTRY PRODUCTS FS CALIBRATOR 1 VITROS CHEMISTRY PRODUCTS HSCRP PERFORMANCE VERIFIER I, II, AND III

G. Regulatory Information:

1. Regulation section:
   21CFR §866.5270 C-reactive protein immunological test system.
   21CFR §862.1150 Calibrator
   21CFR §862.1660 Assayed Controls
2. Classification:
   Class 2
3. Product Code:
   NQD
   JIT
   JJX
4. Panel:
   Immunology (82)

H. Intended Use:

1. Indication(s) for use:
   VITROS Chemistry Products hsCRP Reagent: For in vitro diagnostic use only. VITROS Chemistry Products hsCRP Reagent is used to quantitatively measure C-reactive protein (CRP) in human serum and plasma. CRP is used

to evaluate the risk of developing coronary heart disease (CHD). The risk of CHD increases with values of CRP that exceed 3 mg/L.

VITROS Chemistry Products Calibrator Kit 17: For in vitro diagnostic use only. VITROS Chemistry Products Calibrator Kit 17 is used in conjunction with VITROS Chemistry Products FS Calibrator 1 to calibrate VITROS 5,1 FS Chemistry Systems for the quantitative measurement of C-reactive protein (CRP) using VITROS hsCRP Reagent.
VITROS Chemistry Products hsCRP Performance Verifiers I, II and III: For in vitro diagnostic use only. VITROS Chemistry Products hsCRP Performance Verifiers are assayed controls used to monitor performance of hsCRP Reagent on VITROS 5,1 FS Chemistry Systems.

2. Special condition for use statement(s):
   Prescription use only

3. Special instrument Requirements:
   VITROS 5,1 FS Chemistry System

I. Device Description:

The VITROS Chemistry Products hsCRP Reagent consists of two wet reagents. Reagent 1 is a buffering solution and Reagent 2 contains latex particles coated with anti-CRP mouse monoclonal antibodies.
The VITROS Chemistry Products Calibrator Kit 17 is composed of stabilized human serum to which human C-reactive protein and preservatives have been added.
The VITROS Chemistry Products FS Calibrator 1 is composed of processed water and sodium chloride.
The VITROS Chemistry Products hsCRP Performance Verifiers consists of human plasma and plasma proteins to which stabilizers and preservatives have been added.
The reagents are combined by the VITROS 5,1 FS Chemistry System to perform the VITROS hsCRP assay.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Dade Behring N High sensitivity CRP assay
   VITROS Chemistry Products CRP Performance Verifiers

2. Predicate K number(s):
   k033908
   k953197

3. Comparison with predicate

Reagent and Calibrators

Device Characteristic	VITROS hsCRP Assay	Dade Behring N High Sensitivity CRP Assay
Intended Use	Quantitative measurement of C-reactive protein (CRP)	Same
Basic principle	Latex particle enhanced Immunoturbidimetry	Particle enhanced immunonephelometry
Traceability	CRM 470	CRM 470
Reagents	Liquid ready to use	Liquid ready to use
Instrumentation	VITROS 5,1 FS Chemistry System	Dade Behring BN ProSpec System
Sample type	Serum and plasma (Heparin)	Serum and plasma (heparin and EDTA)

Controls

Device Characteristic	VITROS hsCRP Performance Verifiers	VITROS CRP Performance Verifiers
Intended Use	VITROS hsCRP Performance Verifiers are assayed controls used to monitor performance of hsCRP Reagent on VITROS 5,1 FS Chemistry Systems.	VITROS CRP Performance Verifier is an assayed control used to monitor performance on VITROS Chemistry Systems.
Matrix	A base matrix of human plasma and plasma proteins to which stabilizers and preservative have been added.	A base matrix of human serum to which purified human C-reactive protein, inorganic salts and preservatives have been added.
Levels	Low, Medium, and High	Low and High

K. Standard/Guidance Document Referenced (if applicable):

NCCLS Guideline EP9-A2 - Method Comparison and Bias Estimation Using Patient Samples

NCCLS Guideline EP5-A - Evaluation of Precision Performance of Clinical Chemistry Devices

NCCLS Guideline EP6-A - Evaluation of the Linearity of Quantitative Analytical Methods

NCCLS Guideline EP7-A - Interference Testing in Clinical Chemistry

L. Test Principle:

Sample is mixed with Reagent 1 containing a buffer. Addition of anti-CRP antibodies coupled to latex microparticles (Reagent 2) produces an immunochemical reaction yielding CRP antigen/antibody complexes. The turbidity is measured spectrophotometrically at 660 nm. Once a calibration has been performed for each reagent lot, the CRP concentration in each unknown sample can be determined using the stored calibration curve and the measured absorbance obtained in the assay of the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Device precision was evaluated according to NCCLS EP5-A. Three control sera assayed in duplicate twice per day for 20 days.

	Conventional and SI Units (mg/L)					
System	Mean Conc.	Within Day SD*	Within Lab SD**	Within Lab CV%**	Number of Observations	Number of Days
VITROS 5,1 FS	0.60	0.014	0.030	5.0%	80	20
	1.84	0.018	0.038	2.1%	80	20
	10.64	0.124	0.187	1.8%	80	20

*Within Day precision was determined using two runs / day with two replications per run.

** Within Lab precision was determined using a single lot of reagents on a single analyzer, calibrating once a week.

b. Linearity/assay reportable range:

The reportable range of the VITROS hsCRP assay is 0.10 to 15.00 mg/L. Results outside this range will appear as <0.10 or >15.00. The reportable ranges are based on linearity studies that show the assay is linear across the measuring range of the assay.

c. Traceability (controls, calibrators, or method):

The standards for value assignment are traceable to IRMM/IFCC CRM470 (RPPHS).

The International Calibrator, CRM470 (RPPHS), is used to create a multi-level series of calibration standards for use on the Dade Behring nephelometric method for CRP. A panel of human specimens, assayed with the Dade Behring nephelometric method, are used as secondary calibrators to standardize the VITROS hsCRP assay on the VITROS 5,1 FS Chemistry System. The VITROS hsCRP assay on the VITROS 5,1 FS Chemistry System, calibrated with an assayed panel of human specimens, is used to value-assign master lots of calibrators, which are used as working calibrators to value-assign production lots of calibrators.

d. Detection limit:

The lower limit of detection (0.1 mg/L) is based on the functional sensitivity of the assay, which is defined as the concentration of CRP that results in a 20% Coefficient of Variation (CV).

e. Analytical specificity:

Hemoglobin (up to 1000 mg/dL), bilirubin (up to 50 mg/dL), Intralipid (up to 450 mg/dL), Rheumatoid factor (up to 1200 IU/mL) and 18 exogenous compounds were found to not interfere with the

assay. The list of tested drugs and their concentrations can be found in the package insert.

f. Assay cut-off:
Not Applicable

2. Comparison studies:
   a. Method comparison with predicate device:
   A comparison with the predicate method using 110 serum samples ranging from 0.26 to 14.7 mg/L was performed. The following linear regression equation was obtained:
   VITROS hsCRP assay = 0.954 X + 0.063 mg/L with a correlation coefficient of 0.993, where X is the predicate device.

   b. Matrix comparison:
   Comparison studies between serum samples and samples collected in serum separator tubes and tubes containing the anticoagulant Lithium Heparin were performed. There were no significant differences observed between these sample types.

3. Clinical studies:
   a. Clinical sensitivity:
   Not Applicable

   b. Clinical specificity:
   Not Applicable

   c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range:

Classification for Cardiovascular Disease Risk	Conventional and SI Units (mg/L)
Low	< 1.0
Average	1.0 to < 3.0
High	3.0 to 10.0
Indeterminant*	> 10.0

*May be an indication of another source of inflammation or infection.

The expected values for cardiovascular risk stratification published by the US Dept. of Health and Human Services, Centers for Disease Control and Prevention and the American Heart Association for high sensitivity C-reactive

protein are based on the Dade Behring BN ProSpec nephelometric method for CRP.

Accuracy evaluations were carried out by comparison of results for 195 serum samples (101 females, 94 males) tested with the VITROS Chemistry Products hsCRP assay with those obtained using the Dade Behring BN ProSpec nephelometric method for CRP. The VITROS hsCRP assay results were equivalent to the Dade Behring BN ProSpec nephelometric method results. Therefore, the published classification ranges are applicable to the VITROS Chemistry Products hsCRP assay.

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.